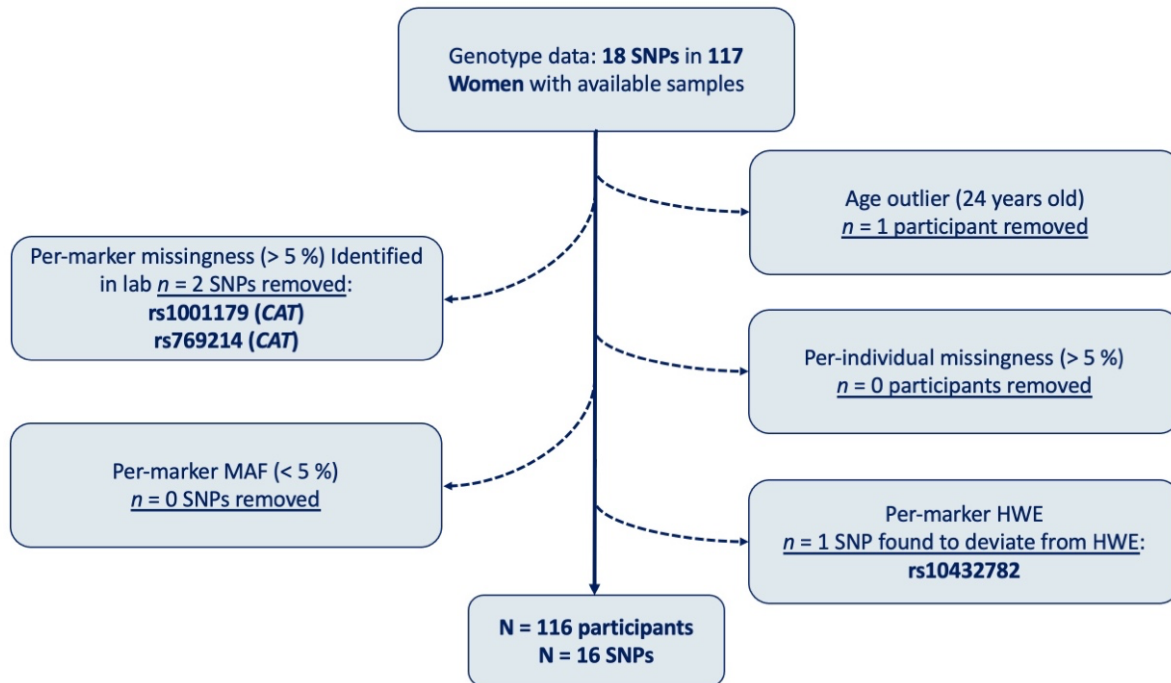


Supplemental Figure 1. Quality Control and Data Screening Pipeline



Supplemental Table 1. CpG Sites and CRF Occurrence Significant Results

N = 116 Participants at study entry				n = 96 Additional pretreatment sub analysis			
Gene	CpG	OR	p-value	Gene	CpG	OR	p-value
<i>NFE2L2</i>	cg12647821	8.816	0.049	<i>NFE2L2</i>	cg12647821	23.997	0.027
<i>PRDX1</i>	cg09131901	0.012	0.028	<i>PRDX1</i>	cg09131901	0.006	0.049
<i>SOD2</i>	cg10002977	15.807	0.023	-	-	-	-

Note. Inclusion of all participants (N = 116) Compared to participants who did not have chemotherapy and/or aromatase inhibitor therapy prior to study entry (n = 96).

Abbreviations. *NFE2L2*, Nuclear factor erythroid 2-related factor 2; *PRDX1*, Peroxiredoxin 1; *SOD2*, Superoxide dismutase 2

Supplemental Table 2. CpG Sites and CRF Severity Significant Results

N = 116 Participants at study entry				n = 96 Additional pretreatment sub analysis			
Gene	CpG	Beta	p-value	Gene	CpG	Beta	p-value
<i>NFE2L2</i>	cg15956152	2.267	0.016	<i>NFE2L2</i>	cg15956152	2.347	0.003
<i>NFE2L2</i>	cg21382890	1.909	0.022				
				<i>NFE2L2</i>	cg25268435	2.187	0.049
<i>PRDX1</i>	cg15627031	1.718	0.007	<i>PRDX1</i>	cg15627031	1.681	0.010
<i>PRDX1</i>	cg22820568	4.552	0.008	<i>PRDX1</i>	cg22820568	4.658	0.027
<i>PRDX1</i>	cg09131901	3.978	0.042				
<i>TXN</i>	cg14509895	1.952	0.019	<i>TXN</i>	cg14509895	2.630	0.011
<i>KEAP1</i>	cg12095186	3.836	0.024				
				<i>KEAP1</i>	cg01289804	-2.379	0.021
<i>SOD2</i>	cg14515483	1.688	0.039	<i>SOD2</i>	cg14515483	1.664	0.049

Note. Inclusion of all participants (N = 116) Compared to participants who did not have chemotherapy and/or aromatase inhibitor therapy prior to study entry (n = 96).

Abbreviations. *NFE2L2*, Nuclear factor erythroid 2-related factor 2; *PRDX1*, Peroxiredoxin 1; *TXN*, Thioredoxin Reductase 1; *KEAP1*, Kelch-like ECH-associated protein 1; *SOD2*, Superoxide dismutase 2

Supplemental Table 3. SNPs and CRF Occurrence Significant Results

N = 116 Participants at study entry				n = 96 Additional pretreatment sub analysis			
Gene	SNP	OR	p-value	Gene	SNP	OR	p-value
<i>NFE2L2</i>	rs2706110	8.816	0.049	-	-	-	-
<i>SOD1</i>	rs10432782	0.318	0.038	<i>SOD1</i>	rs10432782	0.205	0.029

Note. Inclusion of all participants (N = 116) Compared to participants who did not have chemotherapy and/or aromatase inhibitor therapy prior to study entry (n = 96). There were no significant SNPs in the context of CRF severity for either analysis.

Abbreviations. *CAT*, Catalase; *KEAP1*, Kelch-like ECH-associated protein 1; *NFE2L2*, Nuclear factor erythroid 2-related factor 2; *PRDX1*, Peroxiredoxin 1; *SOD1*, Superoxide dismutase 1; *SOD2*, Superoxide dismutase 2; *TXN*, Thioredoxin Reductase 1

Supplemental Table 4. Covariate Analysis Results

Potential Covariates	Covariates included in models		Pearson Correlation Coefficient	95% CI	p-value
	A Priori	Data-Driven			
Age	X		-0.176	-0.35 - 0.02	0.072
Maximal Oxygen Consumption [VO _{2 max}] (ml/kg/min)		X	0.240	0.03 - 0.43	0.023
Body Mass Index (kg/m ²)		X	0.212	0.00 - 0.40	0.043
Employment			0.085	-0.11 - 0.27	0.384
Married or Living with Partner			-0.255	-0.43 - -0.07	0.009
Parental Status			0.029	-0.16 - 0.22	0.765
State Area Deprivation Index Decile			0.049	-0.14 - 0.24	0.616
National Area Deprivation Index Percentile			0.089	-0.10 - 0.27	0.363

Radiation Therapy			-0.125	-0.31 - 0.07	0.203
Chemotherapy			-0.016	-0.21 - 0.18	0.871
Pain Interference		X	0.366	0.19 - 0.52	0.000
Pain Severity			0.233	0.04 - 0.41	0.017
Anxiety		X	0.494	0.33 - 0.62	0.000
Depression		X	0.517	0.36 - 0.64	0.000
Daytime Sleepiness		X	0.516	0.36 - 0.64	0.000
Perceived Cognitive Function			0.396	0.22 - 0.55	0.000

Abbreviations. CI, Confidence Interval; kg/m², kilograms per square meter; ml/kg/min, milliliter per kilogram per minute

Supplemental Table 5. CpG Sites and CRF Occurrence Analysis Adjusted Logistic Regression

Results

Gene	CpG Sites	OR	Statistic	p- value	Lower 95% CI	Upper 95 % CI	FDR
<i>SOD2</i>	cg10002977	15.8068	2.2700	0.0232	1.5930	204.1432	0.9982
<i>PRDX1</i>	cg09131901	0.0121	-2.2041	0.0275	0.0002	0.4790	0.9982
<i>NFE2L2</i>	cg12647821	8.8163	1.9656	0.0493	1.1516	93.6413	0.9982
<i>NFE2L2</i>	cg21334654	5.4146	1.9597	0.0500	1.0730	33.0196	0.9982
<i>TXN</i>	cg14509895	5.5519	1.9341	0.0531	1.0854	37.4553	0.9982
<i>SOD1</i>	cg17017569	5.9606	1.8835	0.0596	1.0158	43.8806	0.9982
<i>NFE2L2</i>	cg25268435	5.8328	1.8416	0.0655	0.9792	44.9703	0.9982
<i>PRDX1</i>	cg03501596	3.6796	1.8325	0.0669	1.0841	17.2269	0.9982
<i>NFE2L2</i>	cg03314080	2.6703	1.8203	0.0687	0.9853	8.4694	0.9982
<i>CAT</i>	cg20234170	0.3885	-1.7573	0.0789	0.1210	1.0311	0.9982
<i>NFE2L2</i>	cg15956152	5.6642	1.7226	0.0850	0.8814	50.4036	0.9982
<i>PRDX1</i>	cg22820568	30.6887	1.7201	0.0854	0.7219	1983.5795	0.9982

<i>NFE2L2</i>	cg05303734	18.7559	1.6362	0.1018	0.6023	795.9721	0.9982
<i>PRDX1</i>	cg08483560	9.1796	1.5467	0.1219	0.6692	196.8924	0.9982
<i>SOD1</i>	cg18841894	3.7853	1.5417	0.1232	0.7648	23.6798	0.9982
<i>NFE2L2</i>	cg02507578	4.0327	1.5415	0.1232	0.7239	26.7739	0.9982
<i>PRDX1</i>	cg15627031	2.5585	1.4948	0.1350	0.7155	9.1837	0.9982
<i>KEAP1</i>	cg12095186	0.0752	-1.4049	0.1600	0.0014	2.1251	0.9982
<i>NFE2L2</i>	cg06141123	3.5692	1.3578	0.1745	0.6010	25.6510	0.9982
<i>CAT</i>	cg00894715	0.4359	-1.3427	0.1794	0.1215	1.4283	0.9982
<i>NFE2L2</i>	cg07613405	1.9239	1.3318	0.1829	0.7385	5.2229	0.9982
<i>PRDX1</i>	cg06530443	0.1949	-1.3149	0.1885	0.0131	1.8486	0.9982
<i>NFE2L2</i>	cg21392576	0.7204	-1.3062	0.1915	0.4322	1.1789	0.9982
<i>CAT</i>	cg20049007	0.1650	-1.3046	0.1920	0.0091	2.2078	0.9982
<i>NFE2L2</i>	cg21382890	2.3397	1.2614	0.2072	0.5998	9.6257	0.9982
<i>KEAP1</i>	cg07695362	0.1168	-1.2493	0.2116	0.0034	3.2527	0.9982
<i>KEAP1</i>	cg24892871	0.1617	-1.2391	0.2153	0.0077	2.5299	0.9982
<i>SOD1</i>	cg16086310	9.0644	1.2351	0.2168	0.3357	413.7695	0.9982

<i>NFE2L2</i>	cg09248506	0.1904	-1.2282	0.2194	0.0115	2.4944	0.9982
<i>TXN</i>	cg19102983	0.2008	-1.2173	0.2235	0.0133	2.6438	0.9982
<i>SOD1</i>	cg16129213	13.4306	1.2109	0.2259	0.2271	1143.0526	0.9982
<i>CAT</i>	cg07431921	0.2632	-1.1298	0.2586	0.0233	2.5240	0.9982
<i>SOD1</i>	cg02533120	5.6588	1.1162	0.2643	0.2737	133.9474	0.9982
<i>SOD2</i>	cg14515483	1.9054	1.0865	0.2772	0.5495	6.2848	0.9982
<i>KEAP1</i>	cg06008936	0.3242	-1.0844	0.2782	0.0375	2.3533	0.9982
<i>TXN</i>	cg07804122	0.4082	-1.0794	0.2804	0.0726	1.9733	0.9982
<i>CAT</i>	cg02564456	0.7211	-1.0711	0.2841	0.3837	1.2959	0.9982
<i>TXN</i>	cg18874458	6.4432	1.0658	0.2865	0.2338	244.2405	0.9982
<i>KEAP1</i>	cg26988016	0.3226	-1.0444	0.2963	0.0338	2.5158	0.9982
<i>KEAP1</i>	cg01289804	0.3711	-1.0357	0.3003	0.0554	2.6883	0.9982
<i>KEAP1</i>	cg17759293	4.2325	1.0199	0.3078	0.2675	75.0250	0.9982
<i>NFE2L2</i>	cg17300868	2.2918	1.0180	0.3087	0.4844	12.2358	0.9982
<i>KEAP1</i>	cg09841779	0.4469	-1.0118	0.3116	0.0338	1.1528	0.9982
<i>KEAP1</i>	cg03890664	0.3755	-1.0100	0.3125	0.0511	2.4669	0.9982

<i>SOD1</i>	cg06470379	3.3456	0.9806	0.3268	0.2827	39.2790	0.9982
<i>CAT</i>	cg00127788	0.4409	-0.9682	0.3329	0.0777	2.2374	0.9982
<i>NFE2L2</i>	cg11542063	0.4381	-0.9653	0.3344	0.0788	2.3965	0.9982
<i>SOD2</i>	cg10124975	0.5571	-0.9362	0.3492	0.1598	2.1132	0.9982
<i>NFE2L2</i>	cg20042412	0.2781	-0.9338	0.3504	0.0157	3.7508	0.9982
<i>PRDX1</i>	cg21319693	1.9420	0.8895	0.3737	0.4020	8.7092	0.9982
<i>KEAP1</i>	cg00522555	0.2550	-0.8819	0.3778	0.0102	4.8964	0.9982
<i>PRDX1</i>	cg18894049	0.3612	-0.8761	0.3810	0.0259	1.8189	0.9982
<i>CAT</i>	cg20731136	0.7537	-0.8585	0.3906	0.3777	1.4197	0.9982
<i>KEAP1</i>	cg15676203	4.8251	0.8548	0.3926	0.1299	203.8725	0.9982
<i>CAT</i>	cg07768201	0.7577	-0.7896	0.4298	0.3688	1.5009	0.9982
<i>SOD1</i>	cg03338682	2.9438	0.7739	0.4390	0.1970	50.7302	0.9982
<i>NFE2L2</i>	cg09183072	0.5259	-0.7732	0.4394	0.0920	2.5483	0.9982
<i>SOD1</i>	cg17253939	2.9433	0.7590	0.4479	0.2101	59.9688	0.9982
<i>KEAP1</i>	cg02337283	0.4299	-0.7568	0.4492	0.0475	4.0471	0.9982
<i>CAT</i>	cg03728580	0.5973	-0.7553	0.4501	0.1450	2.2015	0.9982

<i>PRDX1</i>	cg02881230	0.2503	-0.7483	0.4543	0.0055	8.7411	0.9982
<i>KEAP1</i>	cg01018726	0.1459	-0.7476	0.4547	0.0006	17.4787	0.9982
<i>SOD2</i>	cg06346099	2.2647	0.7349	0.4624	0.2552	21.6059	0.9982
<i>PRDX1</i>	cg21268223	0.5591	-0.7149	0.4747	0.1148	3.2466	0.9982
<i>SOD1</i>	cg18126791	2.4078	0.7133	0.4757	0.2288	30.8151	0.9982
<i>CAT</i>	cg25060988	0.6740	-0.7131	0.4758	0.2137	1.9647	0.9982
<i>CAT</i>	cg17034036	0.6505	-0.7116	0.4767	0.1746	1.6838	0.9982
<i>PRDX1</i>	cg17149431	2.0940	0.6764	0.4988	0.2482	18.8397	0.9982
<i>NFE2L2</i>	cg26271591	1.8640	0.6507	0.5152	0.2834	12.7822	0.9982
<i>CAT</i>	cg02109652	0.8135	-0.6374	0.5239	0.4229	1.5381	0.9982
<i>NFE2L2</i>	cg21570130	1.9722	0.6234	0.5330	0.2419	18.3757	0.9982
<i>PRDX1</i>	cg14219630	1.7133	0.6203	0.5351	0.3161	10.0198	0.9982
<i>CAT</i>	cg26483667	0.4861	-0.6122	0.5404	0.0462	4.9021	0.9982
<i>KEAP1</i>	cg25142576	2.1348	0.6003	0.5483	0.1914	29.0047	0.9982
<i>NFE2L2</i>	cg14787953	0.3766	-0.5845	0.5589	0.0146	11.8014	0.9982
<i>PRDX1</i>	cg01680661	0.4871	-0.5695	0.5690	0.0374	5.6940	0.9982

<i>PRDX1</i>	cg23411172	2.1828	0.5464	0.5848	0.1351	39.8451	0.9982
<i>PRDX1</i>	cg06070002	1.5940	0.5415	0.5882	0.3021	9.4873	0.9982
<i>SOD2</i>	cg04239613	1.2934	0.5298	0.5963	0.5018	3.4649	0.9982
<i>CAT</i>	cg01847719	0.9039	-0.5296	0.5964	0.6139	1.3130	0.9982
<i>NFE2L2</i>	cg08113064	0.6656	-0.5164	0.6056	0.1362	3.1346	0.9982
<i>TXN</i>	cg01206539	1.7612	0.5082	0.6113	0.1961	16.5888	0.9982
<i>CAT</i>	cg24099074	0.8045	-0.5008	0.6165	0.3331	1.8848	0.9982
<i>TXN</i>	cg22966348	1.3266	0.4944	0.6210	0.3497	3.8016	0.9982
<i>NFE2L2</i>	cg15827767	1.7253	0.4687	0.6393	0.1758	18.1688	0.9982
<i>PRDX1</i>	cg00361201	2.1739	0.4430	0.6578	0.0738	80.7659	0.9982
<i>KEAP1</i>	cg06911149	2.2686	0.4396	0.6602	0.0598	98.8830	0.9982
<i>SOD1</i>	cg05363872	0.6860	-0.4362	0.6627	0.1123	3.6431	0.9982
<i>NFE2L2</i>	cg22397783	1.4382	0.4311	0.6664	0.2707	7.7301	0.9982
<i>NFE2L2</i>	cg01357409	2.2895	0.4187	0.6754	0.0461	120.2242	0.9982
<i>NFE2L2</i>	cg02858143	1.1233	0.4166	0.6770	0.6280	2.0441	0.9982
<i>CAT</i>	cg03720043	0.8794	-0.4165	0.6770	0.4662	1.5950	0.9982

<i>SOD1</i>	cg26893544	1.6481	0.4125	0.6800	0.1346	17.1945	0.9982
<i>CAT</i>	cg26588072	1.9087	0.4030	0.6870	0.0802	47.5550	0.9982
<i>CAT</i>	cg00734966	1.5846	0.3959	0.6922	0.1603	16.2420	0.9982
<i>SOD1</i>	cg20813486	1.5669	0.3954	0.6926	0.1581	14.4992	0.9982
<i>CAT</i>	cg23760576	0.7332	-0.3848	0.7004	0.1387	3.4445	0.9982
<i>TXN</i>	cg13176083	0.5980	-0.3800	0.7039	0.0314	6.7509	0.9982
<i>PRDX1</i>	cg07159951	1.5844	0.3370	0.7361	0.1010	23.2067	0.9982
<i>KEAP1</i>	cg26500801	0.7088	-0.3270	0.7437	0.0855	5.6743	0.9982
<i>NFE2L2</i>	cg27507284	0.7640	-0.3269	0.7438	0.1507	3.9937	0.9982
<i>NFE2L2</i>	cg15735209	1.4914	0.3247	0.7454	0.1269	17.1518	0.9982
<i>PRDX1</i>	cg19937480	0.6768	-0.3171	0.7512	0.0589	7.8775	0.9982
<i>PRDX1</i>	cg02631906	1.2926	0.3114	0.7555	0.2518	6.6644	0.9982
<i>PRDX1</i>	cg13622147	0.6352	-0.3064	0.7593	0.0313	11.7607	0.9982
<i>NFE2L2</i>	cg08334199	1.7077	0.3037	0.7614	0.0478	56.4042	0.9982
<i>SOD1</i>	cg13151889	1.2124	0.2989	0.7650	0.3500	4.5667	0.9982
<i>NFE2L2</i>	cg01417537	1.3135	0.2929	0.7696	0.2076	8.4520	0.9982

<i>NFE2L2</i>	cg06493556	1.4781	0.2758	0.7827	0.0845	23.9472	0.9982
<i>TXN</i>	cg26246296	0.7882	-0.2569	0.7973	0.1236	4.9044	0.9982
<i>KEAP1</i>	cg12465942	0.8036	-0.2487	0.8036	0.1387	4.5740	0.9982
<i>NFE2L2</i>	cg14958951	0.7535	-0.2404	0.8100	0.0681	7.0815	0.9982
<i>CAT</i>	cg18155366	0.7242	-0.2369	0.8127	0.0456	10.3610	0.9982
<i>TXN</i>	cg13843427	0.8231	-0.2273	0.8202	0.1478	4.4801	0.9982
<i>CAT</i>	cg07801620	1.1329	0.2257	0.8214	0.3868	3.4634	0.9982
<i>KEAP1</i>	cg03754063	1.5533	0.2133	0.8311	0.0273	100.7484	0.9982
<i>KEAP1</i>	cg20226327	0.7265	-0.2089	0.8345	0.0263	14.2348	0.9982
<i>NFE2L2</i>	cg22451100	0.9313	-0.2000	0.8415	0.3352	1.7026	0.9982
<i>TXN</i>	cg19078334	0.8950	-0.1826	0.8551	0.2032	2.6265	0.9982
<i>CAT</i>	cg17876896	0.8216	-0.1796	0.8575	0.0896	7.0422	0.9982
<i>PRDX1</i>	cg21462146	0.9563	-0.1724	0.8632	0.5633	1.5889	0.9982
<i>SOD1</i>	cg14206710	0.8130	-0.1475	0.8827	0.0460	12.5261	0.9982
<i>SOD1</i>	cg03173570	1.1898	0.1350	0.8926	0.0943	15.9618	0.9982
<i>KEAP1</i>	cg18005170	0.8742	-0.1041	0.9171	0.0655	11.6150	0.9982

<i>SOD1</i>	cg19948014	0.8941	-0.0999	0.9204	0.0964	8.3348	0.9982
<i>NFE2L2</i>	cg20247600	0.9180	-0.0952	0.9242	0.1508	5.4051	0.9982
<i>PRDX1</i>	cg06989253	1.1245	0.0875	0.9303	0.0723	14.7716	0.9982
<i>SOD1</i>	cg00966890	0.8757	-0.0854	0.9320	0.0404	19.6951	0.9982
<i>NFE2L2</i>	cg13344867	0.9065	-0.0695	0.9446	0.0512	14.0766	0.9982
<i>SOD1</i>	cg19949530	1.0907	0.0680	0.9458	0.0795	12.6666	0.9982
<i>KEAP1</i>	cg10505024	0.9178	-0.0615	0.9510	0.0545	13.8154	0.9982
<i>NFE2L2</i>	cg03988329	1.0478	0.0449	0.9642	0.1374	8.7521	0.9982
<i>PRDX1</i>	cg20112865	1.0291	0.0302	0.9759	0.1535	6.7961	0.9982
<i>CAT</i>	cg06027906	0.9876	-0.0250	0.9800	0.3629	2.6381	0.9982
<i>KEAP1</i>	cg01586432	0.9664	-0.0226	0.9819	0.0475	20.1827	0.9982
<i>KEAP1</i>	cg02428100	1.0202	0.0223	0.9822	0.1367	5.0859	0.9982
<i>KEAP1</i>	cg22779878	0.9794	-0.0170	0.9865	0.0834	11.0580	0.9982
<i>PRDX1</i>	cg11833889	0.9959	-0.0128	0.9898	0.5120	1.8342	0.9982
<i>KEAP1</i>	cg25801292	1.0116	0.0124	0.9901	0.1599	6.3208	0.9982
<i>SOD2</i>	cg03398387	1.0036	0.0043	0.9965	0.2004	5.1594	0.9982

<i>CAT</i>	cg20552529	0.9972	-0.0024	0.9981	0.0979	9.4634	0.9982
<i>CAT</i>	cg17098995	1.0027	0.0022	0.9982	0.0923	12.0792	0.9982

Note. CpG sites are sorted by smallest *p*-value.

Abbreviations. *CAT*, Catalase; *KEAP1*, Kelch-like ECH-associated protein 1; *NFE2L2*, Nuclear factor erythroid 2-related factor 2; *PRDX1*, Peroxiredoxin 1; *SOD1*, Superoxide dismutase 1; *SOD2*, Superoxide dismutase 2; *TXN*, Thioredoxin Reductase 1; OR, Odds Ratio, CI, Confidence Interval; FDR, False Discovery Rate.

Supplemental Table 6. CpG Sites and CRF Severity Analysis Adjusted Linear Regression

Results

Gene	CpG Sites	b	Statistic	p- value	Lower 95% CI	Upper 95 % CI	FDR
<i>PRDX1</i>	cg15627031	1.7183	2.8010	0.0066	1.3842	8.2418	0.5396
<i>PRDX1</i>	cg22820568	4.5523	2.7523	0.0076	3.4452	21.6133	0.5396
<i>NFE2L2</i>	cg15956152	2.2673	2.4793	0.0156	1.0971	10.1459	0.5751
<i>TXN</i>	cg14509895	1.9520	2.4050	0.0189	0.7994	8.5898	0.5751
<i>NFE2L2</i>	cg21382890	1.9086	2.3519	0.0216	0.6803	8.2972	0.5751
<i>KEAP1</i>	cg12095186	3.8359	-2.3046	0.0243	-16.4945	-1.1856	0.5751
<i>SOD2</i>	cg14515483	1.6878	2.1050	0.0390	0.1849	6.9207	0.7420
<i>PRDX1</i>	cg09131901	3.9782	-2.0750	0.0418	-16.1930	-0.3162	0.7420
<i>SOD2</i>	cg10002977	3.0510	1.9172	0.0594	-0.2388	11.9376	0.8296
<i>NFE2L2</i>	cg25268435	2.1871	1.9106	0.0603	-0.1857	8.5429	0.8296
<i>PRDX1</i>	cg21268223	2.2297	-1.8180	0.0735	-8.5030	0.3956	0.8296
<i>KEAP1</i>	cg01289804	2.6014	-1.8172	0.0736	-9.9180	0.4639	0.8296
<i>TXN</i>	cg22966348	1.5520	1.7761	0.0802	-0.3405	5.8533	0.8296

<i>SOD1</i>	cg17017569	2.1495	1.7657	0.0819	-0.4938	8.0847	0.8296
<i>KEAP1</i>	cg02337283	2.8599	-1.6948	0.0947	-10.5541	0.8598	0.8296
<i>KEAP1</i>	cg09841779	1.1773	-1.6610	0.1013	-4.3047	0.3937	0.8296
<i>KEAP1</i>	cg24892871	3.4416	-1.6280	0.1081	-12.4705	1.2646	0.8296
<i>SOD2</i>	cg06346099	3.0128	1.6205	0.1097	-1.1296	10.8942	0.8296
<i>KEAP1</i>	cg06911149	4.5003	1.6148	0.1110	-1.7133	16.2472	0.8296
<i>TXN</i>	cg19102983	3.1927	-1.5620	0.1229	-11.3579	1.3838	0.8392
<i>NFE2L2</i>	cg21570130	2.6623	1.5572	0.1241	-1.1668	9.4583	0.8392
<i>SOD2</i>	cg10124975	1.7209	-1.5138	0.1347	-6.0391	0.8290	0.8694
<i>CAT</i>	cg20049007	3.1106	-1.4686	0.1465	-10.7755	1.6388	0.9045
<i>KEAP1</i>	cg02428100	2.2315	1.4289	0.1576	-1.2643	7.6416	0.9135
<i>KEAP1</i>	cg00522555	4.1024	-1.4063	0.1642	-13.9555	2.4168	0.9135
<i>KEAP1</i>	cg06008936	2.5466	-1.3580	0.1789	-8.5400	1.6233	0.9135
<i>TXN</i>	cg26246296	2.6034	1.2981	0.1986	-1.8155	8.5746	0.9135
<i>CAT</i>	cg00127788	2.0858	-1.2896	0.2015	-6.8519	1.4722	0.9135
<i>NFE2L2</i>	cg21334654	2.0274	1.2730	0.2074	-1.4648	6.6264	0.9135

<i>CAT</i>	cg07431921	2.9632	-1.2711	0.2080	-9.6795	2.1464	0.9135
<i>PRDX1</i>	cg21319693	2.1256	1.2593	0.2122	-1.5648	6.9183	0.9135
<i>KEAP1</i>	cg17759293	3.4714	1.2096	0.2306	-2.7279	11.1260	0.9135
<i>SOD1</i>	cg26893544	3.1898	1.1989	0.2347	-2.5409	10.1893	0.9135
<i>PRDX1</i>	cg01680661	3.3581	-1.1929	0.2371	-10.7068	2.6952	0.9135
<i>SOD1</i>	cg16086310	4.4195	1.1876	0.2391	-3.5706	14.0674	0.9135
<i>PRDX1</i>	cg23411172	3.7440	1.1855	0.2400	-3.0326	11.9096	0.9135
<i>CAT</i>	cg26483667	2.7353	-1.1839	0.2406	-8.6965	2.2199	0.9135
<i>NFE2L2</i>	cg11542063	2.2846	-1.1495	0.2544	-7.1850	1.9328	0.9135
<i>KEAP1</i>	cg12465942	2.3242	-1.1200	0.2666	-7.2409	2.0347	0.9135
<i>CAT</i>	cg17034036	1.0325	-1.0746	0.2864	-3.1699	0.9508	0.9135
<i>NFE2L2</i>	cg26271591	2.4621	1.0297	0.3068	-2.3779	7.4481	0.9135
<i>CAT</i>	cg00894715	1.5643	-1.0172	0.3127	-4.7126	1.5304	0.9135
<i>CAT</i>	cg20552529	2.9476	-0.9831	0.3291	-8.7795	2.9841	0.9135
<i>NFE2L2</i>	cg12647821	2.2753	0.9596	0.3407	-2.3570	6.7237	0.9135
<i>CAT</i>	cg00734966	2.8984	-0.9555	0.3427	-8.5530	3.0141	0.9135

<i>PRDX1</i>	cg03501596	1.3726	0.9345	0.3533	-1.4563	4.0218	0.9135
<i>SOD1</i>	cg17253939	3.4280	0.9294	0.3559	-3.6543	10.0266	0.9135
<i>NFE2L2</i>	cg14787953	4.1825	-0.8918	0.3756	-12.0762	4.6159	0.9135
<i>NFE2L2</i>	cg01357409	5.1288	0.8897	0.3767	-5.6711	14.7978	0.9135
<i>SOD1</i>	cg03338682	3.3163	0.8812	0.3813	-3.6953	9.5398	0.9135
<i>NFE2L2</i>	cg09248506	3.4684	-0.8764	0.3839	-9.9607	3.8815	0.9135
<i>NFE2L2</i>	cg15827767	3.1278	0.8587	0.3935	-3.5556	8.9272	0.9135
<i>NFE2L2</i>	cg06141123	2.4467	0.8561	0.3949	-2.7876	6.9770	0.9135
<i>NFE2L2</i>	cg22397783	2.2639	0.8359	0.4061	-2.6251	6.4099	0.9135
<i>PRDX1</i>	cg19937480	3.2463	-0.8307	0.4091	-9.1746	3.7812	0.9135
<i>SOD1</i>	cg13151889	1.6389	0.8157	0.4175	-1.9335	4.6074	0.9135
<i>NFE2L2</i>	cg21392576	0.6740	-0.8145	0.4182	-1.8940	0.7960	0.9135
<i>TXN</i>	cg01206539	2.8073	0.7995	0.4268	-3.3573	7.8464	0.9135
<i>SOD1</i>	cg02533120	4.1334	0.7941	0.4299	-4.9657	11.5305	0.9135
<i>KEAP1</i>	cg10505024	3.5645	-0.7904	0.4321	-9.9302	4.2956	0.9135
<i>NFE2L2</i>	cg01417537	2.4709	0.7890	0.4328	-2.9810	6.8803	0.9135

<i>KEAP1</i>	cg25142576	3.2391	0.7630	0.4481	-3.9919	8.9350	0.9135
<i>PRDX1</i>	cg06989253	3.3673	-0.7602	0.4498	-9.2791	4.1595	0.9135
<i>NFE2L2</i>	cg03314080	1.1914	0.7583	0.4509	-1.4741	3.2809	0.9135
<i>SOD1</i>	cg18126791	3.1572	0.7575	0.4514	-3.9085	8.6918	0.9135
<i>KEAP1</i>	cg07695362	4.0463	-0.7260	0.4703	-11.0117	5.1367	0.9135
<i>PRDX1</i>	cg18894049	1.9296	-0.7185	0.4749	-5.2369	2.4640	0.9135
<i>SOD1</i>	cg19948014	2.7431	0.7115	0.4792	-3.5220	7.4254	0.9135
<i>PRDX1</i>	cg00361201	4.2983	-0.7076	0.4816	-11.6185	5.5356	0.9135
<i>CAT</i>	cg23760576	2.1336	-0.6952	0.4893	-5.7409	2.7743	0.9135
<i>NFE2L2</i>	cg08334199	4.2709	0.6932	0.4905	-5.5618	11.4830	0.9135
<i>PRDX1</i>	cg11833889	0.7694	0.6787	0.4997	-1.0131	2.0574	0.9135
<i>KEAP1</i>	cg20226327	4.1765	-0.6691	0.5057	-11.1287	5.5396	0.9135
<i>PRDX1</i>	cg06530443	2.5625	-0.6686	0.5060	-6.8266	3.4001	0.9135
<i>KEAP1</i>	cg25801292	2.5298	0.6569	0.5135	-3.3863	6.7100	0.9135
<i>KEAP1</i>	cg18005170	3.6355	-0.6504	0.5176	-9.6191	4.8898	0.9135
<i>KEAP1</i>	cg15676203	5.0991	0.6466	0.5201	-6.8780	13.4722	0.9135

<i>TXN</i>	cg19078334	1.5866	0.6296	0.5311	-2.1672	4.1650	0.9135
<i>KEAP1</i>	cg26988016	2.5936	-0.6167	0.5395	-6.7748	3.5761	0.9135
<i>PRDX1</i>	cg06070002	2.1845	0.6089	0.5446	-3.0290	5.6891	0.9135
<i>PRDX1</i>	cg17149431	2.7883	-0.6002	0.5504	-7.2375	3.8904	0.9135
<i>NFE2L2</i>	cg20042412	3.5105	-0.5928	0.5553	-9.0863	4.9240	0.9135
<i>NFE2L2</i>	cg03988329	2.7480	0.5726	0.5688	-3.9099	7.0570	0.9135
<i>CAT</i>	cg26588072	4.1190	-0.5528	0.5822	-10.4965	5.9422	0.9135
<i>PRDX1</i>	cg02881230	4.3962	-0.5470	0.5862	-11.1770	6.3679	0.9135
<i>NFE2L2</i>	cg14958951	2.9706	0.5369	0.5931	-4.3328	7.5227	0.9135
<i>CAT</i>	cg24099074	1.1727	0.5335	0.5954	-1.7750	1.6417	0.9135
<i>KEAP1</i>	cg22779878	3.0712	-0.5256	0.6009	-7.7426	4.5145	0.9135
<i>CAT</i>	cg18155366	3.3489	-0.5221	0.6033	-8.4311	4.9341	0.9135
<i>PRDX1</i>	cg20112865	2.3660	-0.5106	0.6113	-5.9294	3.5131	0.9135
<i>KEAP1</i>	cg26500801	2.9218	0.5076	0.6134	-4.3473	7.3134	0.9135
<i>SOD1</i>	cg05363872	2.3908	-0.4909	0.6251	-5.9444	3.5972	0.9135
<i>SOD1</i>	cg16129213	5.2967	0.4906	0.6253	-7.9708	13.1679	0.9135

<i>NFE2L2</i>	cg20247600	2.3407	0.4709	0.6392	-3.5686	5.7732	0.9135
<i>CAT</i>	cg03720043	0.8109	0.4700	0.6399	-1.8594	1.6271	0.9135
<i>NFE2L2</i>	cg02507578	2.2958	0.4694	0.6403	-3.5034	5.6588	0.9135
<i>NFE2L2</i>	cg07613405	1.1432	-0.4656	0.6430	-2.8136	1.7489	0.9135
<i>CAT</i>	cg20234170	1.1891	-0.4651	0.6433	-2.9258	1.8197	0.9135
<i>PRDX1</i>	cg02631906	2.1557	0.4502	0.6540	-3.3312	5.2723	0.9135
<i>SOD1</i>	cg20813486	2.9530	-0.4468	0.6564	-7.2122	4.5731	0.9135
<i>CAT</i>	cg06027906	1.3465	0.4204	0.6755	-1.9389	1.8232	0.9135
<i>KEAP1</i>	cg03890664	2.4968	0.4195	0.6762	-3.9348	6.0296	0.9135
<i>NFE2L2</i>	cg22451100	0.8974	0.4047	0.6869	-1.4275	2.1539	0.9135
<i>SOD2</i>	cg04239613	1.3083	-0.3873	0.6997	-3.1173	2.1039	0.9135
<i>SOD1</i>	cg14206710	3.6023	0.3820	0.7036	-5.8122	8.5644	0.9135
<i>TXN</i>	cg13176083	3.0671	-0.3642	0.7168	-7.2375	5.0032	0.9135
<i>PRDX1</i>	cg14219630	2.2384	0.3551	0.7236	-3.6719	5.2614	0.9135
<i>CAT</i>	cg07801620	1.3719	-0.3548	0.7239	-3.2243	2.2509	0.9135
<i>NFE2L2</i>	cg13344867	3.4328	-0.3385	0.7360	-8.0120	5.6879	0.9135

<i>NFE2L2</i>	cg27507284	2.0974	0.3352	0.7385	-3.4823	4.8884	0.9135
<i>PRDX1</i>	cg07159951	3.5969	0.3207	0.7494	-6.0240	8.3311	0.9135
<i>SOD1</i>	cg06470379	3.2254	0.3192	0.7506	-5.4067	7.4657	0.9135
<i>NFE2L2</i>	cg05303734	4.4918	0.3072	0.7596	-7.5833	10.3434	0.9135
<i>NFE2L2</i>	cg02858143	0.7527	-0.3061	0.7605	-1.7324	1.2716	0.9135
<i>NFE2L2</i>	cg17300868	1.9782	-0.2988	0.7660	-4.5384	3.3564	0.9135
<i>CAT</i>	cg01847719	0.5186	0.2925	0.7708	-0.8832	1.1866	0.9135
<i>KEAP1</i>	cg01586432	3.7848	-0.2813	0.7794	-8.6169	6.4879	0.9135
<i>SOD1</i>	cg00966890	4.1811	-0.2795	0.7807	-9.5117	7.1746	0.9135
<i>SOD1</i>	cg18841894	2.0137	0.2793	0.7809	-3.4559	4.5808	0.9135
<i>KEAP1</i>	cg03754063	5.4396	-0.2782	0.7817	-12.3675	9.3414	0.9135
<i>PRDX1</i>	cg13622147	3.9575	-0.2744	0.7846	-8.9829	6.8111	0.9135
<i>PRDX1</i>	cg21462146	0.6831	-0.2742	0.7848	-1.5503	1.1758	0.9135
<i>CAT</i>	cg17098995	3.3036	-0.2466	0.8059	-7.4069	5.7774	0.9300
<i>NFE2L2</i>	cg06493556	3.4847	-0.2239	0.8235	-7.7340	6.1732	0.9300
<i>NFE2L2</i>	cg08113064	2.0063	-0.2149	0.8305	-4.4348	3.5724	0.9300

<i>KEAP1</i>	cg01018726	6.4324	0.2017	0.8407	-11.5380	14.1332	0.9300
<i>TXN</i>	cg07804122	2.1410	0.1972	0.8443	-3.8501	4.6946	0.9300
<i>SOD1</i>	cg03173570	3.4183	0.1892	0.8505	-6.1745	7.4677	0.9300
<i>TXN</i>	cg18874458	4.4987	-0.1763	0.8606	-9.7703	8.1837	0.9300
<i>CAT</i>	cg03728580	1.8189	0.1759	0.8609	-3.3096	3.9496	0.9300
<i>TXN</i>	cg13843427	2.2814	-0.1720	0.8640	-4.9449	4.1603	0.9300
<i>CAT</i>	cg25060988	1.4554	-0.1694	0.8660	-1.5646	1.6551	0.9300
<i>CAT</i>	cg17876896	2.8034	0.1598	0.8735	-5.1461	6.0422	0.9300
<i>PRDX1</i>	cg08483560	3.0793	0.1545	0.8776	-5.6687	6.6204	0.9300
<i>NFE2L2</i>	cg09183072	2.2691	-0.1458	0.8845	-4.8587	4.1971	0.9303
<i>CAT</i>	cg02109652	0.8736	-0.1329	0.8946	-0.8832	1.1866	0.9303
<i>SOD2</i>	cg03398387	2.0357	0.1293	0.8975	-3.7990	4.3254	0.9303
<i>CAT</i>	cg20731136	0.8561	-0.0779	0.9382	-2.1208	3.2531	0.9654
<i>CAT</i>	cg07768201	0.9427	-0.0613	0.9513	-1.2370	1.9993	0.9690
<i>CAT</i>	cg02564456	0.8068	0.0561	0.9554	-1.7145	2.9657	0.9690
<i>NFE2L2</i>	cg15735209	3.3058	0.0309	0.9755	-6.4945	6.6986	0.9757

<i>SOD1</i>	cg19949530	3.4150	-0.0305	0.9757	-6.9188	6.7102	0.9757
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To Note: CpG sites are sorted by smallest *p*-value.

Abbreviations. *CAT*, Catalase; *KEAP1*, Kelch-like ECH-associated protein 1; *NFE2L2*, Nuclear factor erythroid 2-related factor 2; *PRDX1*, Peroxiredoxin 1; *SOD1*, Superoxide dismutase 1; *SOD2*, Superoxide dismutase 2; *TXN*, Thioredoxin Reductase 1; *b*, Beta Coefficient; *CI*, Confidence Interval; *FDR*, False Discovery Rate

Supplemental Table 7. SNPs and CRF Occurrence Analysis Adjusted
Logistic Regression Results

Gene	SNP	OR	Lower 95% CI	Upper 95% CI	p-value	FDR
<i>NFE2L2</i>	rs2706110	3.5404	1.2841	11.0691	0.0201	0.2448
<i>SOD1</i>	rs10432782	0.3181	0.1932	1.6972	0.0376	0.2448
<i>TNX</i>	rs4135225	0.4463	0.1863	0.9951	0.0558	0.2448
<i>PRDX1</i>	rs713358	2.4131	0.9914	6.3944	0.0612	0.2448
<i>KEAP1</i>	rs9676881	0.5706	0.2565	1.2128	0.1521	0.4867
<i>KEAP1</i>	rs1048290	0.6384	0.2951	1.3385	0.2392	0.6379
<i>TNX</i>	rs2301241	0.6974	0.3159	1.5043	0.3596	0.7820
<i>CAT</i>	rs511895	1.4537	0.6211	3.5086	0.3910	0.7820
<i>SOD2</i>	rs4880	0.7869	0.3677	1.6320	0.5234	0.8792
<i>SOD1</i>	rs1041740	1.2885	0.5681	3.0501	0.5495	0.8792
<i>CAT</i>	rs566979	0.8245	0.3796	1.8033	0.6233	0.8883
<i>PRDX1</i>	rs7522705	0.8952	0.4039	1.9687	0.7817	0.8883
<i>PRDX1</i>	rs945179	1.1234	0.4910	2.6120	0.7824	0.8883
<i>CAT</i>	rs525938	0.9054	0.3982	2.0515	0.8101	0.8883
<i>SOD2</i>	rs8031	1.0823	0.5187	2.2944	0.8328	0.8883
<i>SOD2</i>	rs5746136	0.9729	0.4081	2.2389	0.9489	0.9489

To Note. CpG sites are sorted by smallest p-value.

Abbreviations. *CAT*, Catalase; *KEAP1*, Kelch-like ECH-associated protein 1; *NFE2L2*, Nuclear factor erythroid 2-related factor 2; *PRDX1*, Peroxiredoxin 1; *SOD1*, Superoxide dismutase 1; *SOD2*,

Superoxide dismutase 2; *TXN*, Thioredoxin Reductase 1; SNP, Single Nucleotide Polymorphism; OR, Odd Ratio; CI, Confidence Interval; FDR, False Discovery Rate

1 **Supplemental Table 8.** SNPs and CRF Severity Adjusted Linear Regression Analysis Results

Gene	SNP	b	Lower 95% CI	Upper 95% CI	p-value	FDR
<i>TXN</i>	rs4135225	-1.67393	-3.9820	0.6342	0.15282	0.6589
<i>SOD2</i>	rs4880	-1.40489	-3.4432	0.6334	0.1740	0.6589
<i>NFE2L2</i>	rs2706110	1.75782	-0.8317	4.3473	0.18039	0.6589
<i>PRDX1</i>	rs713358	1.54865	-0.8227	3.9200	0.19737	0.6589
<i>TXN</i>	rs2301241	-1.40572	-3.5995	0.7881	0.2059	0.6589
<i>SOD1</i>	rs10432782	-1.43551	-4.0840	1.2130	0.28395	0.7476
<i>SOD2</i>	rs8031	0.93644	-1.1359	3.0088	0.37115	0.7476
<i>SOD1</i>	rs1041740	1.0250	-1.2559	3.3060	0.37378	0.7476
<i>SOD2</i>	rs5746136	0.90119	-1.5233	3.3256	0.46158	0.7499
<i>PRDX1</i>	rs7522705	-0.79823	-2.9803	1.3839	0.46869	0.7499
<i>CAT</i>	rs525938	-0.61946	-2.9753	1.7363	0.60217	0.8147
<i>KEAP1</i>	rs9676881	-0.55911	-2.7382	1.6200	0.6110	0.8147
<i>KEAP1</i>	rs1048290	-0.3683	-2.5311	1.7945	0.73555	0.8937

<i>CAT</i>	rs511895	0.28607	-2.2016	2.7737	0.81954	0.8937
<i>CAT</i>	rs566979	0.22737	-1.9766	2.4313	0.83783	0.8937
<i>PRDX1</i>	rs945179	0.08255	-2.1879	2.3530	0.94249	0.9425

2 *To Note.* CpG sites are sorted by smallest *p*-value.

3 *Abbreviations.* *CAT*, Catalase; *KEAP1*, Kelch-like ECH-associated protein 1; *NFE2L2*, Nuclear
4 factor erythroid 2-related factor 2; *PRDX1*, Peroxiredoxin 1; *SOD1*, Superoxide dismutase
5 1; *SOD2*, Superoxide dismutase 2; *TXN*, Thioredoxin Reductase 1; SNP, Single Nucleotide
6 Polymorphism; *b*; Beta Coefficient; CI, Confidence Interval; FDR, False Discovery Rate.

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